

WHAT IS CLAIMED IS:

1    1. A method for producing a non-human animal model of a human or non-human  
2    animal disease which comprises transferring at least one aberrant form of at least one  
3    gene known to be associated with said disease in humans or non-human animals into  
4    appropriate tissue of a living non-human animal under conditions which result in the  
5    expression of said at least one aberrant gene, wherein said transferring does not require  
6    the modification of the germ-line of said living animal.

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1    2. The method according to claim 1 wherein said human or non-human animal  
2    disease is a neurodegenerative disease.

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1    3. The method according to claim 2 wherein said human disease is selected from the  
2    group consisting of Alzheimer's Disease, Parkinson's Disease, and Huntington's Disease.

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1    4. The method according to claim 3 wherein said at least one gene is an aberrant  
2    form of tau.

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1    5. The method according to claim 3 wherein said aberrant form of tau is P301L,  
2    associated with "fronto-temporal dementia with Parkinson's linked to chromosome 17  
3    (FTDP-17)".

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1    6. The method according to claim 3 wherein said at least one gene is an aberrant  
2    form of alpha-synuclein.

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1    7. The method according to claim 6 wherein said aberrant form of alpha-synuclein is  
2    mutant  $\alpha$ -synuclein (A30P), associated with Parkinson's Disease.

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1    8. The method according to claim 3 wherein said at least one gene is a mutant  
2    amyloid precursor protein (APP), a mutant presenilin-1 (PS1), or combinations thereof,  
3    associated with Alzheimer's Disease.

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1       9.     The method according to claim 1 which comprises identifying a combination of  
2     genes relevant to a particular human pathology and somatically transferring combinations  
3     of said genes into tissues appropriate to said particular human pathology in a non-human  
4     animal model appropriate to said human pathology.

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1       10.    The method according to claim 1 comprising:

2           (a) controlling the location to which the genes are transferred, that is spatially  
3              controlling gene expression of the transferred genes, in the non-human animal  
4              model to which said at least one gene is transferred;

5           (b) controlling the temporal effects of transferred genes at specific times in the  
6              development of otherwise normal organisms, or in the development of organisms  
7              in which germline modifications have previously been made, by selecting the time  
8              at which said transferred genes are introduced into said organism, or by  
9              controlling the time of expression of said transferred genes;

10          (c) evaluating the effects of expression of combinations of multiple transgenes, which  
11             in a germline transgenic non-human animal would be difficult if not impossible to  
12             achieve due to diseases which might prevent the animal model from maturing to  
13             the age-appropriate state for modeling onset of a particular, complex human  
14             disease; 

15          (d) increasing the rate for analyzing multiple genes which contribute to complex,  
16             multifactorial human diseases by transferring more than a single gene into an  
17             appropriate non-human animal model for said disease;

18          (e) testing pharmaceutical agents for their ability to ameliorate specific diseases  
19             induced in said non-human animal model;

20          (f) studying specific human pathologies induced in said non-human animal model by  
21             inducing said pathology in said animal model by transferring said at least one  
22             gene into said animal model;

23          (g) supplementing an existing germline transgenic model with additional somatically  
24             provided gene products to modulate the transgenic model;

25          (h) creating a disease condition in an otherwise healthy animal; and

26          (i) combinations of (a) –(h).

1 11. A non-human animal produced by the method of claim 1.

1 12. A pharmaceutical identified through testing of pharmaceutical compounds

2 using the non-human animal produced according to claim 11.

1 13. A method for inducing neurofibrillary tangles in the brain of a non-human

2 animal which comprises injecting into the brain of said animal an effective amount of

3 a gene expression construct encoding tau, alpha-synuclein, presenilin-1, amyloid

4 precursor protein, IL6, or a combination thereof.

1 14. A non-human animal produced according to the method of claim 13.

1 15. A method for inducing behavioral changes in a non-human animal model

2 which comprises somatic administration of at least one gene directly to the brain of

3 said non-human animal, wherein said at least one gene is associated with a human

4 neurodegenerative disease. B

1 16. The method according to claim 1 wherein said at least one aberrant form

2 of said at least one gene is transferred by means of an adeno-associated virus.

1 17. A composition comprising at least one gene construct adapted for

2 producing a non-human animal model of a human or non-human-animal disease by

3 transferring at least one aberrant form of at least one gene known to be associated

4 with said disease in humans or non-human animals into appropriate tissue of a living

5 non-human animal under conditions which result in the expression of said at least one

6 aberrant gene, wherein said transferring does not require the modification of the

7 germ-line of said living animal, said composition comprising said at least one

8 aberrant gene in a vector construct which results in active expression of said gene

9 upon introduction into said tissue.

1       18.       The composition according to claim 17 wherein said at least one gene is  
2                  an aberrant form of tau.

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1       19.       The composition according to claim 18 wherein said aberrant form of tau  
2                  is P301L, associated with "fronto-temporal dementia with Parkinson's linked to  
3                  chromosome 17 (FTDP-17)".

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1       20.       The composition according to claim 17 wherein said at least one gene is  
2                  an aberrant form of alpha-synuclein.

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1       21..       The composition according to claim 20 wherein said aberrant form of  
2                  alpha-synuclein is mutant  $\alpha$ -synuclein (A30P), associated with Parkinson's Disease.

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1       22..       The composition according to claim 17 wherein said at least one gene is a  
2                  mutant amyloid precursor protein (APP), a mutant presenilin-1 (PS1), or  
3                  combinations thereof, associated with Alzheimer's Disease.

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